

Amendments to the Claims

This listing of the claims replaces all prior versions of the claims in the application.

Listing of claims:

1.-33. (Canceled)

34. (Currently Amended) A hepatitis C virus (HCV) vaccine comprising at least two epitopes, each from a different hotspot epitope, wherein a hotspot epitope is defined as an epitope containing at least one of an epitope of each of the following peptides:

KFPGGGQIVGGVYLLPRRGPRLGVRATRK (SEQ ID NO:73);
GYKVLVLNPSVAAT (SEQ ID NO:60),
AYAAQGYKVLVLNPSVAAT (SEQ ID NO:14),
DLMGYIP(A/L)VGAPL (SEQ ID NO:25; SEQ ID NO:26),
GEVQVVSTATQSFLATCINGVCWTV (SEQ ID NO:49),
HMWNFISGIQYLAGLSTLPGNPA (SEQ ID NO:63),
VDYPYRLWHYPCT(V/I)N(F/Y)TIFK(V/I)RMYVGGVEHRL (SEQ ID NO:132; SEQ ID NO:133; SEQ ID NO:134; SEQ ID NO:135; SEQ ID NO:136; SEQ ID NO:137; SEQ ID NO:138; SEQ ID NO:139; SEQ ID NO:140; SEQ ID NO:141),,
AAWYELTPAETTVRLR (SEQ ID NO:4),
GQGWRLAPITAYSQQTRGLLGCIIV (SEQ ID NO:54),
IGLGKVLVDILAGYGAGVAGALVAFK (SEQ ID NO:70),
FTDNSSPPAVPQTFQV (SEQ ID NO:46),
LEDNRDRSELSPLLLSTTEW (SEQ ID NO:80),
YLVAYQATVCARAQAPPPSWD (SEQ ID NO:149),
MSTNPKPQRKTKRNTNR (SEQ ID NO:93),
LINTNGSWHINRTALNCNDSL (SEQ ID NO:84),
TTILGIGTVLDQAET (SEQ ID NO:125),
FDS(S/V)VLCECYDAG(A/C)AWYE (SEQ ID NO:40; SEQ ID NO:41; SEQ ID NO:42; SEQ ID NO:43; SEQ ID NO:44),
ARLIVFPDLGVRVCEKMALY (SEQ ID NO:8),
AFCSAMYVGDLCGSV (SEQ ID NO:5),

GVLFGLAYFSMVGW (SEQ ID NO:56),
VVCCSMSYTWGTGALITPC (SEQ ID NO:144),
TRVPYFVRAQGLIRA (SEQ ID NO:123) and
TTLLFNILGGWVAAQ (SEQ ID NO:126) and
CINGVCWTV (SEQ ID NO:17).

35-38. (Canceled)

39. (Currently Amended) The HCV vaccine of claim 34, wherein the epitopes are at least two of further comprising an epitope of at least one of the following peptides:

KFPGGGQIVGGVYLLPRRGPRLGVRATRK (SEQ ID NO:73),
KFPGGGQIVGGVYLLPRRGPRL (SEQ ID NO:72), YLLPRRGPRL (SEQ ID NO:146),
LPRRGPRL (SEQ ID NO:86), GPRLGVRAT (SEQ ID NO:50), RLGVRATRK (SEQ ID
NO:103), GYKVLVLNPSVAAT (SEQ ID NO:60), AYAAQGYKVL (SEQ ID NO:9),
AYAAQGYKVLVLNPSVAAT (SEQ ID NO:14); DLMGYIPAV (SEQ ID NO:19),
GYIPLVGAPL (SEQ ID NO:59), DLMGYIPLVGAPL (SEQ ID NO:25), ~~CINGVCWTV~~
(SEQ ID NO:17), GEVQVVSTATQSFLAT (SEQ ID NO:47),
GEVQVVSTATQSFLATCINGVCWTV (SEQ ID NO:49),
~~HMWNFISGIQYLAGLSTLPGNPA~~ (SEQ ID NO:63), MWNFISGIQYLAGLSTLPGN
(SEQ ID NO:94), NFISGIQYLAGLSTLPGNPA (SEQ ID NO:97), QYLAGLSTL (SEQ
ID NO:101), HMWNFISGI (SEQ ID NO:61),
VDYPYRLWHYPCTVNFTIFKVRMYVGGVEHRL (SEQ ID NO:132),
DYPYRLWHYPCTVNFTIFKI (SEQ ID NO:35), DYPYRLWHYPCTVNFTIFKV (SEQ
ID NO:36), VDYPYRLWHYPCTVNYTIFKIRMYVGGVEHRL (SEQ ID NO:135),
DYPYRLWHYPCTVNYTIFKI (SEQ ID NO:38), DYPYRLWHY (SEQ ID NO:33),
TVNYTIFKI (SEQ ID NO:129), TINYTIFK (SEQ ID NO:120), TVNFTIFKV (SEQ ID
NO:127), HYPCTVNYTI (SEQ ID NO:67), HYPCTVNFTI (SEQ ID NO:66),
RMYVGGVEHR (SEQ ID NO:106), AAWEYELTPAETTVRLR (SEQ ID NO:4),
TPAETTVRL (SEQ ID NO:121), GWRLAPITAYSQQTRGLLGCIV (SEQ ID NO:57),
TAYSQQTRGLLGCIV (SEQ ID NO:116), TAYSQQTRGLLG (SEQ ID NO:115),
GQGWRLAPITAYSQ (SEQ ID NO:52), RLLAPITAY (SEQ ID NO:105),
GQGWRLAPITAYSQQTRGLLGCIV (SEQ ID NO:54),

GQGWRLAPITAYSQQTRGLLG (SEQ ID NO:53), AYSQQTRGLL (SEQ ID NO:16), AYSQQTRGL (SEQ ID NO:15), IGLGKVLVDILAGYGAGVAGALVAFK (SEQ ID NO:70), ILAGYGAGV (SEQ ID NO:71), VAGALVAFK (SEQ ID NO:131), GYGAGVAGAL (SEQ ID NO:58), VVCCSMSYTWGTGALITPC (SEQ ID NO:144), SMSYTWGTGALITP (SEQ ID NO:112), SMSYTWGTGAL (SEQ ID NO:111), SYTWGTGALI (SEQ ID NO:114), FTDNSSPPAVPQTFQV (SEQ ID NO:46), LEDRDRSELSPLLLSTTEW (SEQ ID NO:80), LEDRDRSELSPLLLST (SEQ ID NO:79), RSELSPLLL (SEQ ID NO:108), ELSPLLLST (SEQ ID NO:39), DRDRSELSPL (SEQ ID NO:32), LEDRDRSEL (SEQ ID NO:78), LEDRDRSEL (SEQ ID NO:78), YLVAYQATV CARAQAPPSWD (SEQ ID NO:149), YLVAYQATV (SEQ ID NO:148), MSTNPKPQRKTKRNTNR (SEQ ID NO:93), PQRKTKRNTNR (SEQ ID NO:99), QRKTKRNTN (SEQ ID NO:100), RKTKRNTNR (SEQ ID NO:102), MSTNPKPQR (SEQ ID NO:92), MSTNPKPQK (SEQ ID NO:91), INTNGSWHINRTALNCNDSL (SEQ ID NO:84), NGSWHINRTALNCNDSL (SEQ ID NO:98), LINTNGSWHI (SEQ ID NO:82), RTALNCNDSL (SEQ ID NO:109), LINTNGSWHINRTALN (SEQ ID NO:83), SWHINRTALN (SEQ ID NO:113), TTILGIGTVLDQAET (SEQ ID NO:125), TTILGIGTV (SEQ ID NO:124), TILGIGTVL (SEQ ID NO:119), FDSSVLCECYDAGAAWYE (SEQ ID NO:40; SEQ ID NO:44), FDSSVLCECYDAGCA (SEQ ID NO:45), VLCECYDAGA (SEQ ID NO:142), VVLCECYDAGAAWYE (SEQ ID NO:145), ARLIVFPDLGVRVCEKMALY (SEQ ID NO:8), ARLIVFPDL (SEQ ID NO:7), RLIVFPDLGV (SEQ ID NO:104), RVCEKMALY (SEQ ID NO:110), AFCSAMYVGDL CGSV (SEQ ID NO:5), GVLFGLAYFSMVG NW (SEQ ID NO:56), TRVPYFVRAQGLIRA (SEQ ID NO:123), TTLLFNILGGWVAAQ (SEQ ID NO:126), LLFNILGGWV (SEQ ID NO:85).

40. (Currently Amended) The HCV vaccine of claim 34, further defined as comprising at least one epitope from ~~at least three~~ of the following hotspot epitopes:

KFPGGGQIVGGVYLLPRRGPRLGVRATRK (SEQ ID NO:73),
 AYAAQGYKVLVLNPSVAAT (SEQ ID NO:14),
 DLMGYIP(A/L)VGAPL (SEQ ID NO:25; SEQ ID NO:26), and
 GEVQVVSTATQSFLATCINGVCWTV (SEQ ID NO:49), ~~and~~
~~HMWNFISGIQYLAGLSTLPGNPA (SEQ ID NO:63).~~

41. (Canceled)

42. (Withdrawn - Currently Amended) The HCV vaccine of claim 34, further defined as comprising at least one epitope from ~~at least two of~~ the following hotspot epitopes:

VDYPYRLWHYPCT(V/I)N(F/Y)TIFK(V/I)RMVVGVEHRL (SEQ ID NO:132; SEQ ID NO:133; SEQ ID NO:134; SEQ ID NO:135; SEQ ID NO:136; SEQ ID NO:137; SEQ ID NO:138; SEQ ID NO:139; SEQ ID NO:140; SEQ ID NO:141),
AAWYELTPAETTVRLR (SEQ ID NO:4),
GGGWRLAPITAYSQQTRGLLGCIV (SEQ ID NO:54),
IGLGKVLVDILAGYGAGVAGALVAFK (SEQ ID NO:70),
FTDNSSPPAVPQTFQV (SEQ ID NO:46),
LEDNRSELSPLLLSTTEW (SEQ ID NO:80),
YLVAYQATVCARAQAPPPSWD (SEQ ID NO:149),
MSTNPKPQRKTKRNTNR (SEQ ID NO:93) and
LINTNGSWHINRTALNCNDSL (SEQ ID NO:84).

43-44. (Canceled)

45. (Withdrawn - Currently Amended) The HCV vaccine of claim 34, further defined as comprising at least one epitope from ~~at least two of~~ the following hotspot epitopes:

TTILGIGTVLDQAET (SEQ ID NO:125),
FDS(S/V)VLCECYDAG(A/C)AWYE (SEQ ID NO:40; SEQ ID NO:41; SEQ ID NO:42; SEQ ID NO:43; SEQ ID NO:44),
ARLIVFPDLGVRVCEKMALY (SEQ ID NO:8),
AFCSAMYVGDLCGSV (SEQ ID NO:5),
GVLFGLAYFSMVG NW (SEQ ID NO:56),
TRVPYFVRAQGLIRA (SEQ ID NO:123) and
TTLLFNILGGWVAAQ (SEQ ID NO:126).

46-47. (Canceled)

48. (Currently Amended) The HCV vaccine of claim 34, further ~~defined as~~ comprising at least ~~two~~ one of the following epitopes:

KFPGGGQIVGGVYLLPRRGPRLGVRATRK (SEQ ID NO:73),
DLMGYIPAV (SEQ ID NO:19),
LEDNRSELSPLLLSTTEW (SEQ ID NO:80),
DYPYRLWHYPCTVNFTIFKV (SEQ ID NO:36),
GYKVLVLNPSVAAT (SEQ ID NO:60),
CINGVCWTV (SEQ ID NO:17),
AAWYELTPAETTVRLR (SEQ ID NO:4),
YLVAYQATVCARAQAPPPSWD (SEQ ID NO:149),
TAYSQQTRGLLG (SEQ ID NO:115),
HMWNFISGIQYLAGLSTLPGNPA (SEQ ID NO:63),
IGLGKVLVDILAGYGAGVAGALVAFK (SEQ ID NO:70), and
SMSYTWTGALITP (SEQ ID NO:112).

49-53. (Canceled)

54. (Withdrawn - Currently Amended) The HCV vaccine of claim 48, further defined as comprising at least ~~two~~ one of the following epitopes:

KFPGGGQIVGGVYLLPRRGPRLGVRATRK (SEQ ID NO:73),
DYPYRLWHYPCTVNFTIFKV (SEQ ID NO:36),
AAWYELTPAETTVRLR (SEQ ID NO:4),
TAYSQQTRGLLG (SEQ ID NO:115),
HMWNFISGIQYLAGLSTLPGNPA (SEQ ID NO:63),
IGLGKVLVDILAGYGAGVAGALVAFK (SEQ ID NO:70), and
SMSYTWTGALITP (SEQ ID NO:112).

55-57. (Canceled)

58. (Withdrawn) The HCV vaccine of claim 34, further defined as comprising the epitope KFPGGGQIVGGVYLLPRRGPRLGVRATRK (SEQ ID NO:73).

59. (Withdrawn) The HCV vaccine of claim 34, further defined as comprising the epitope DLMGYIPAV (SEQ ID NO:19).

60. (Previously Presented) The HCV vaccine of claim 34, further defined as comprising the epitope CINGVCWTV (SEQ ID NO:17).

61-62. (Canceled)

63. (Withdrawn) The HCV vaccine of claim 34, further defined as comprising the epitope VVCCSMSYTWGTGALITPC (SEQ ID NO:144).

64-66. (Canceled)

67. (Withdrawn - Currently Amended) The vaccine of claim ~~[[65]]~~34, further defined as comprising the epitope KFPGGGQIVGGVYLLPRRGPR (SEQ ID NO:72).

68. (Withdrawn - Currently Amended) The vaccine of claim ~~[[65]]~~34, further defined as comprising the epitopes DLMGYIPAV (SEQ ID NO:19) and KFPGGGQIVGGVYLLPRRGPR (SEQ ID NO:72).

69. (Withdrawn) The HCV vaccine of claim 34, further defined as comprising a peptide ("Peptide A") comprising a sequence $R_1\text{-XZXX}_N\text{XZX-R}_2$, (SEQ ID NOS:152-156, where N is 3-7, respectively) wherein:

N is a whole number between 3 and 7;

X is a positively charged natural and/or non-natural amino acid residue;

Z is an amino acid residue selected from the group consisting of L, V, I, F and/or W;

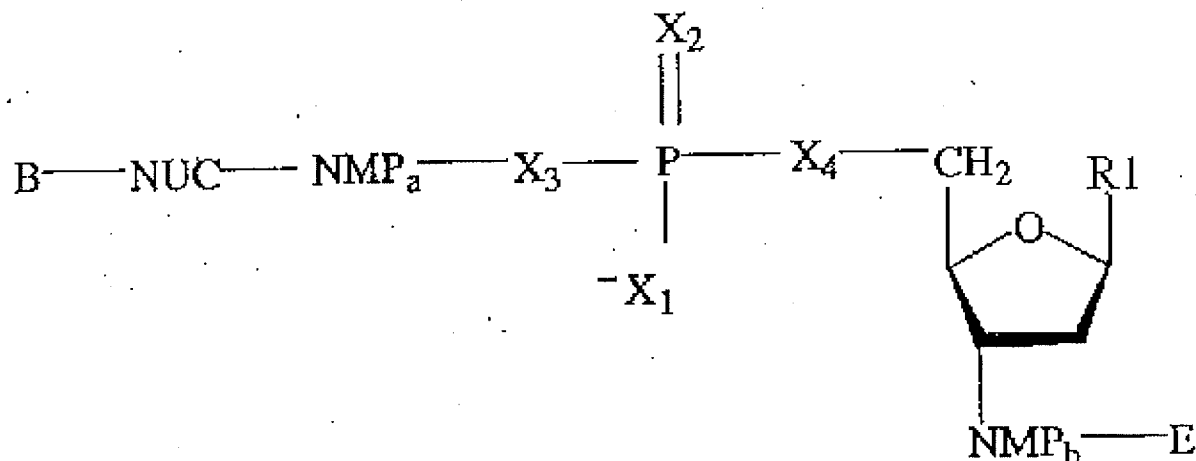
and R_1 and R_2 are independently: -H, -NH₂, -COCH₃, -COH, a peptide with up to 20 amino acid residues or a peptide reactive group, or a peptide linker with or without a peptide; and

$X\text{-R}_2$ may be an amide, ester or thioester of the C-terminal amino acid residue of the peptide.

70. (Canceled)

71. (Withdrawn) The HCV vaccine of claim 69, wherein the sequence of Peptide A is KLKL₅KLK (SEQ ID NO:75).

72. (Previously Presented) The HCV vaccine of claim 34, further defined as comprising an immunostimulatory oligodeoxynucleic acid molecule (ODN) having the structure according to the formula (I):



wherein

R1 is selected from hypoxanthine and uracil;

any X is O or S;

any NMP is a 2' deoxynucleoside monophosphate or monothiophosphate, further defined as: deoxyadenosine-, deoxyguanosine-, deoxyinosine-, deoxycytosine-, deoxyuridine-, deoxythymidine-, 2-methyl-deoxyinosine-, 5-methyl-deoxycytosine-, deoxypseudouridine-, deoxyribosepurine-, 2-amino-deoxyribosepurine-, 6-S-deoxyguanine-, 2-dimethyl-deoxyguanosine-, or N-isopentenyl-deoxyadenosine-monophosphate or -monothiophosphate,

NUC is a 2' deoxynucleoside, further defined as deoxyadenosine-, deoxyguanosine-, deoxyinosine-, deoxycytosine-, deoxythymidine-, 2-methyl-deoxyuridine-, 5-methyl-deoxycytosine-, deoxypseudouridine-, deoxyribosepurine-, 2-amino-deoxyribosepurine-, 6-S-deoxyguanine-, 2-dimethyl-deoxyguanosine-, or N-isopentenyl-deoxyadenosine;

a and b are integers from 0 to 100 with the proviso that a + b is between 4 and 150; and

B and E are common groups for 5' or 3' ends of nucleic acid molecules ("I-/U-ODN").

73. (Previously Presented) The HCV vaccine of claim 72, wherein said I-/U-ODN is oligo d(IC)₁₃.

74. (Canceled)

75. (Withdrawn) The HCV vaccine of claim 34, further defined as comprising a polycationic peptide.

76. (Previously Presented) The HCV vaccine of claim 34, further defined as comprising an oligodeoxynucleotide containing a CpG-motif.

77-84. (Canceled)